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Original Research Article

Strongyloidiasis in Mexico: A Neglected Disease

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Abstract: Strongyloidiasis is a soil-borne disease caused by nematodes of the genus *Strongyloides*. The species most relevant to human health is *S. stercoralis*. The infection can persist for life if left untreated and occurs in various clinical forms, from asymptomatic to death. It mainly affects tropical and subtropical regions, with an estimated 370 million people affected worldwide, including Mexico. The life cycle of this parasite is complex, with free-living and parasitic stages. Infective filariform larvae penetrate intact skin, reach the lungs and are swallowed, developing in the intestine. Diagnosis is challenging and is based on the detection of larvae in biological samples, as well as serological and molecular tests. The main treatment is ivermectin, effective against adult forms, but multiple rounds may be necessary due to the autoinfectious cycle. Immunocompromised people are more susceptible to severe and disseminated infections. The lack of awareness and resources in endemic areas makes timely diagnosis and treatment difficult. Strongyloidiasis is a neglected disease, receiving less attention and funding for research and treatment development. To address it, efforts are required in education, improvement of the health infrastructure, research and prevention strategies.

Keywords: Strongyloidiasis; Nematodes Infections; Neglected Diseases; Mexico.

INTRODUCTION

Strongyloidiasis or strongyloidiasis is a soil-transmitted helminthiasis and represents one of the neglected tropical diseases in the world, it can have a fatal course, especially in immunosuppressed patients, as well as being one of the few infections that can last a lifetime in patients who do not have been treated, as a consequence of underdiagnosis [1]. This disease is caused by nematodes that belong to:

Phylum: Nematoda
Class: Secernentea
Order: Rhabditida
Family: *Strongyloididae*

The genus contains more than 50 species that can infect different birds, reptiles or amphibians; however, *S. stercoralis* is considered the species of greatest medical importance due to its cosmopolitan distribution, although there are also cases of human infection by *S. fuelleborni fuelleborni* (endemic to Africa) and *S. fuelleborni kelleyi* (endemic to Papua New Guinea) [2- 4].

Currently it is estimated that this disease affects about 370 million people worldwide, mainly inhabitants of tropical and subtropical regions; Mexico is considered one of the endemic countries. Migration from endemic areas has allowed the appearance of imported cases in developed countries [5].

DEVELOPMENT

Historical Background

Previously, this nematode was named *Anguillulosia* by Bavay in 1876, being the first to

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describe its free and parasitic way of life (intestinal worms), in addition to the fact that in the same year Normand, a French doctor, is the first to find the parasite in feces of soldiers in Cochinchina (today Vietnam) suffering from severe diarrhea, later in 1877 Grassi described some of the different larval phases that the parasite develops during its biological cycle, this when studying biopsies of 5 French soldiers who died in Cochinchina [4- 6].

Epidemiology

– **World**

This disease is endemic to tropical and subtropical countries, although there are also low endemic sites with temperate climates. It is estimated that worldwide it has a prevalence of 8.1%, being more affected in places with low socioeconomic levels [7- 9]. The most affected areas are Southeast Asia, Western Pacific, Africa, Latin America, Southeast United States, and Australia. Currently it is estimated that there are between 100 and 370 million people infected in the world; however, these data are unknown precisely [10, 11]. (FIGURE 1).

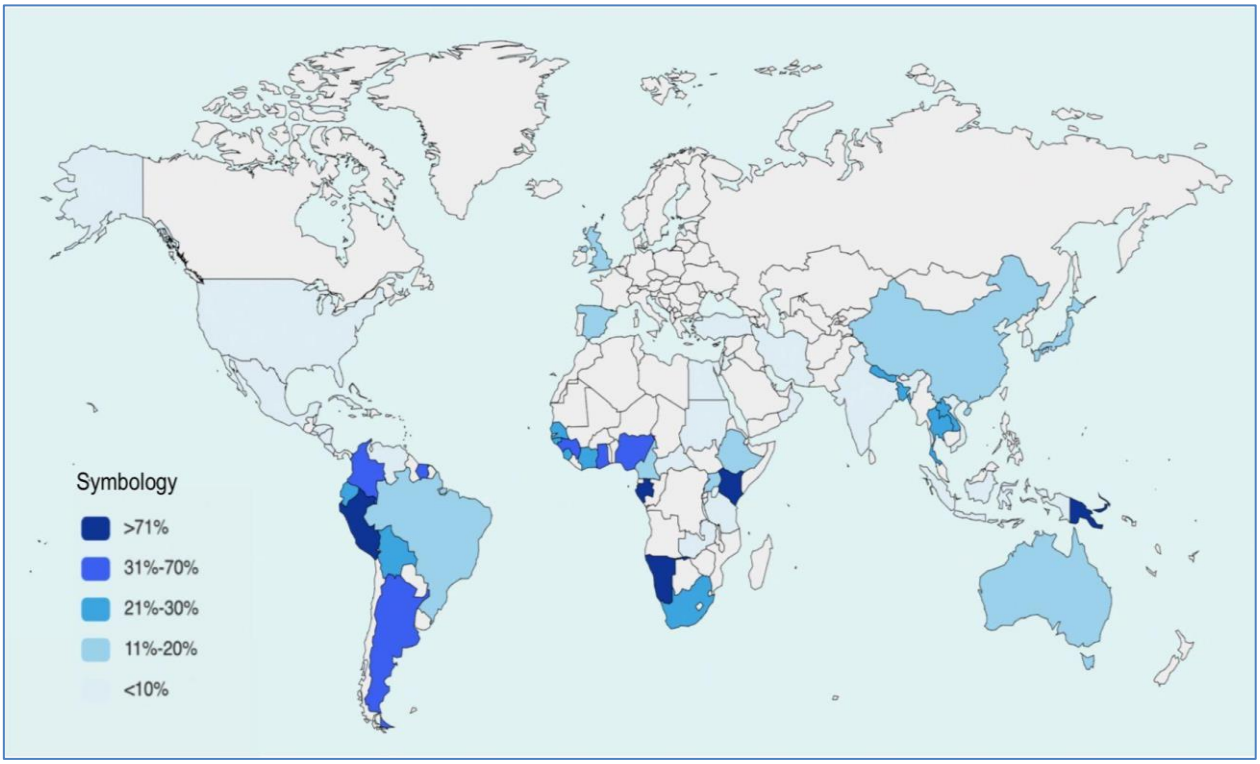

Figure 1: Worldwide prevalence of *S. stercoralis* . (Own elaboration adapted from Schär *et al., Plos Negl Trop Dis.* 2013; 11:7(7). Available at: https://doi.org/10.1371/journal.pntd.0002288)

It is important to highlight that there are reports of patients coinfected with the human lymphotropic virus 1 (HTLV-1), since both etiological agents share endemic regions such as Japan, Jamaica and South America [2- 5].

– **Mexico**

According to the work carried out by Tay *et al.*, in 1976, the global prevalence for Mexico was 4.3% [5- 12]. Currently there are few epidemiological data, so the prevalence is estimated between 0.1% and 68% [13].

By consulting national and foreign medical-scientific journals by more than 30 academic search engines, including PubMed, Google Scholar, Scielo, Dialnet, Redalyc, Doaj, Scopus, Latindex, etc; 11 publications related to *S. stercoralis* in our territory were obtained in the period from 2000 to 2022. One of these corresponds to a clinical case in a pediatric patient from Guerrero [10], 7 to clinical cases in adults [5- 17], and 3 reports of the prevalence in studies of particular populations [4- 19]. (TABLE 1)

Author	Year	Description
PEDIATRIC		
Vazquez O, *et al.*, [10]	2002	Case report of an 11-year-old boy, originally from Guerrero, who underwent laparoscopy and established the diagnosis of gastrointestinal zygomycosis, in addition to intestinal maceration by sedimentation examination by the Ritchie method, in which abundant larvae of *S. stercoralis.*
ADULTS		
Ochoa MD, *et al.*, [6]	2003	Case report of a 55-year-old male patient with a previous diagnosis of asthma without successful treatment with bronchodilators. Given a picture of acute dyspnea, multiple nodules are evident in the light of the airways by bronchoscopy, an analysis of bronchoalveolar lavage and feces is performed where *S. stercoralis* larvae are visualized. In the autopsy, parasitic specimens are found in the bronchial nodules.
Ugarte A, *et al.*, [13]	2006	Case report of the first case of disseminated strongyloidiasis in Mexico, in a 45-year-old patient with generalized lupus erythematosus and immunosuppressive treatment. It presents as a picture of acute abdomen, severe sepsis, and *Escherichia coli* pneumonia.
Rodriguez M, *et al.*, [5]	2012	Case report of hyperinfection syndrome in a patient with late-onset HIV infection, with secondary involvement of the central nervous system by *Cryptococcus neoformans*.
Romero R, *et al.*, [14]	2012	Case report of disseminated strongyloidiasis in a 49-year-old male patient, with a previous diagnosis of HIV, resulting in stomach involvement and intestinal perforation, in addition to secondary sepsis.
Sanchez JT, *et al.*, [16]	2019	Case report of a 76-year-old female patient residing in the State of Mexico, with previous diagnoses of diabetes mellitus, hypertension, hypothyroidism, obesity, empty sella syndrome, and panhypopituitarism, which led to treatment with prednisone. Shortly after starting treatment, it shows eosinophilia in multiple studies and a large number of rhabditiform larvae compatible with *S. stercoralis* are evidenced through stool examinations.
Rodriguez EG, *et al.*, [15]	2020	Case report of hyperinfection syndrome in a 40-year-old male patient from Monterrey, with a previous diagnosis of diabetes mellitus and a history of long-standing alcoholism, these being identified as risk factors.
Pérez MA, *et al.*, [17]	2021	Case report of a 37-year-old male patient, who began with acute respiratory symptoms after diarrhea and the diagnosis of Crohn's disease was erroneously established. Biopsies of the stomach and duodenum were performed where *S. stercoralis.*
SPECIAL POPULATIONS		
Guevara Y, *et al.*, [4]	2003	Study that aims to determine the prevalence of enteroparasites in 420 people from indigenous and mestizo communities in the Sierra de Nayarit, in which 2 cases of strongyloidiasis are reported in indigenous people and 1 among mestizos.
Rodriguez EG, *et al.*, [18]	2019	Study that aimed to determine intestinal parasitism in 56 HIV-immunocompromised patients (seropositive and seronegative) with diarrhea in a hospital in Monterrey. The total prevalence of parasitism was 64%, and only 1 case of strongyloidiasis was reported.
Sánchez JT, *et al.*, [19]	2021	Study that aimed to determine intestinal parasitosis in 600 HIV+ patients in a concentration hospital in CDMX, in which 2 cases of strongyloidiasis with involvement of the bronchial tree are reported.

Table 1: Report of Strongyloides stercoralis cases in Mexico from 2000-2022

Risk Factor's

Rainfall is the most important geographical factor, since humid soils, little rain and shade (for example, mines, coffee and banana plantations) are climatic conditions that favor the development of this nematode, on the contrary, in desert areas. Its development is null [3, 4]. Environmental contamination with feces spread by people who defecate at ground level, immigrants, patients in mental institutions, and soldiers allows the spread and survival of this agent. In addition, some conditions specific to the host are important, for example, the disease predominates in adulthood and the male sex [7].

Walking barefoot on soil contaminated with human feces containing larvae increases the risk of infection and is the main mode of transmission, this is more likely in areas with poor sanitation; likewise, people who work in agriculture or land-related occupations, such as gardeners, may be at increased risk of exposure to the parasite due to direct contact with the soil. This nematodiasis has been associated with immunosuppressive diseases such as that caused by the human T-cell lymphotropic virus type 1 (HTLV-1), and to a lesser extent with the human immunodeficiency virus (HIV/AIDS) [11].

It is important to mention the record of cases of Hyperinfection Syndrome or Hyperparasitosis (HS) in patients with recent transplants, under immunosuppressive therapeutic regimen or infection by other agents, which may make them more susceptible to developing this severe form, characterized by the presence of an excessive amount of parasites and their

consequent spread [2- 12]. In the case of corticosteroids, they hinder the Th2 response by binding to glucocorticoid receptors on CD4+ cells (helper lymphocytes) and changing the regular mechanisms of immunity. Immunocompromised patients have a high risk of developing hyperinfection syndrome, but malnutrition, alcoholism, and diabetes mellitus should also be considered as predisposing factors [2- 6].

Etiological Agent

- **Parasitic adult female:** it is approximately 2-3 µm long, finely thin, translucent and its posterior end is blunt. The anterior end is constituted by a hexagonal mouth surrounded by six papillae, this is continued with a long esophagus (covers approximately ⅓ of the total length) and cylindrical, continued by the long and small intestine, this ends in a rectum in which it is Opens anus near posterior end. It is considered diffelpha, because the uterus, oviducts and ovaries are located on both sides of the vulvar opening. It is important to highlight that there is no parasitic adult male because only the female inhabits the intestine, reproducing by parthenogenesis, directly generating fertile eggs. [2- 22].
- **Free-living adult female:** it can measure up to 1 µm in length, they are provided with a striated, thin and translucent cuticle. Its rhabditoid esophagus is formed by 3 parts (anterior cylindrical procorpus, narrow isthmus and posterior rounded bulb), it continues with the intestine and ends in the rectum near the posterior end. The reproductive system is similar to that of the parasitic female, except that each uterus contains a large number of eggs [2- 22].
- **Free-living adult male:** as is characteristic of nematodes, these are smaller, reaching up to 750 µm in length. Its posterior end is characteristically pointed and bending ventrally giving a “J” shape. The esophagus has the same characteristics as those of the female. Its reproductive system is made up of a simple straight tube, at the anterior end there is a blind testicle fused with the vas deferens and then the seminal vesicle; It also has 2 copulatric spicules, which allow it to anchor itself to the female during copulation [2- 22].
- **Egg:** measures approximately 50 µm long by 30-35 µm wide, hyaline and ovoid in shape, later multiple divisions are oviposited and contain a larva inside. Those laid by parasitic and free-living females are practically identical [2- 22].
- **Juvenile stage L1 (rhabditoid larvae):** approximately 180 to 380 µm long, with a high motility index, and a pointed posterior end. Its oral cavity is short and narrow, the radiobioid esophagus is muscular, with a posterior bulb and an isthmus. On the dorsal side of its posterior third there is an elongated genital primordium. (FIGURE 2)

Figure 2: Distal end of a juvenile stage L1 (rhabditoid larva). (Own image)

L2 juvenile stage: these are destined to become infective, hence the name "pre-infectious larva". Your esophagus lengthens and becomes less muscular [2-23].

- **Juvenile stage L3 (infective filariform larva):** it is approximately 600 µm long, finely thin, with a finely striated cuticle and a notch at its distal end that allows its differentiation. The lateral wing extends to the tip of the forked tail, generating a notch, important for the recognition of this agent. The mouth is likely to be closed and impervious to small particles and liquids. The cylindrical esophagus occupies 40% of the larva's length, has no feeding or contractility characteristics and is surrounded by a nerve ring, continuous with a long, straight intestine. The larval cuticle, in addition to protecting the larva, allows it to detect the presence of a host and secrete molecules that allow the invasion [2-22].

Biological Cycle

It comprises a complex life cycle with different stages of development that can be free-living or parasitic, which is why it is divided into:

1. **Free-living cycle (heterogonic, sexual, or indirect):** rhabditiform larvae shed in the feces of infected patients, molt twice to become infective filariform larvae, or may molt four times and become free-living, mating adult

males and females and produce eggs from which rhabditiform larvae hatch, which can give rise to a new generation of free-living adults or infective filariform larvae. Filariform larvae have the ability to penetrate the skin of the human host to initiate the parasitic cycle.

2. **Parasitic cycle (homogonous, asexual or direct):** the filariform larvae present in contaminated soil penetrate human skin, mainly in the feet of people who do not usually wear shoes, and are transported to the lungs where they penetrate the alveolar spaces, later through From the bronchial tree they crawl to the pharynx and esophagus to be swallowed and thus reach the small intestine. In the small intestine they molt twice and become adult females. The females live hooked in the epithelium of the small intestine and through parthenogenesis they produce eggs, which give rise to rhabditiform larvae. Rhabditiform larvae can be eliminated with stools or can generate a state of autoinfection, in which rhabditiform larvae become infective filariform larvae that can penetrate either the intestinal mucosa (internal autoinfection) or the skin of the perianal area. (external autoinfection), to follow the route described above or they can spread widely in the body and generate hyperinfection syndrome [3- 11]. (FIGURE 3).

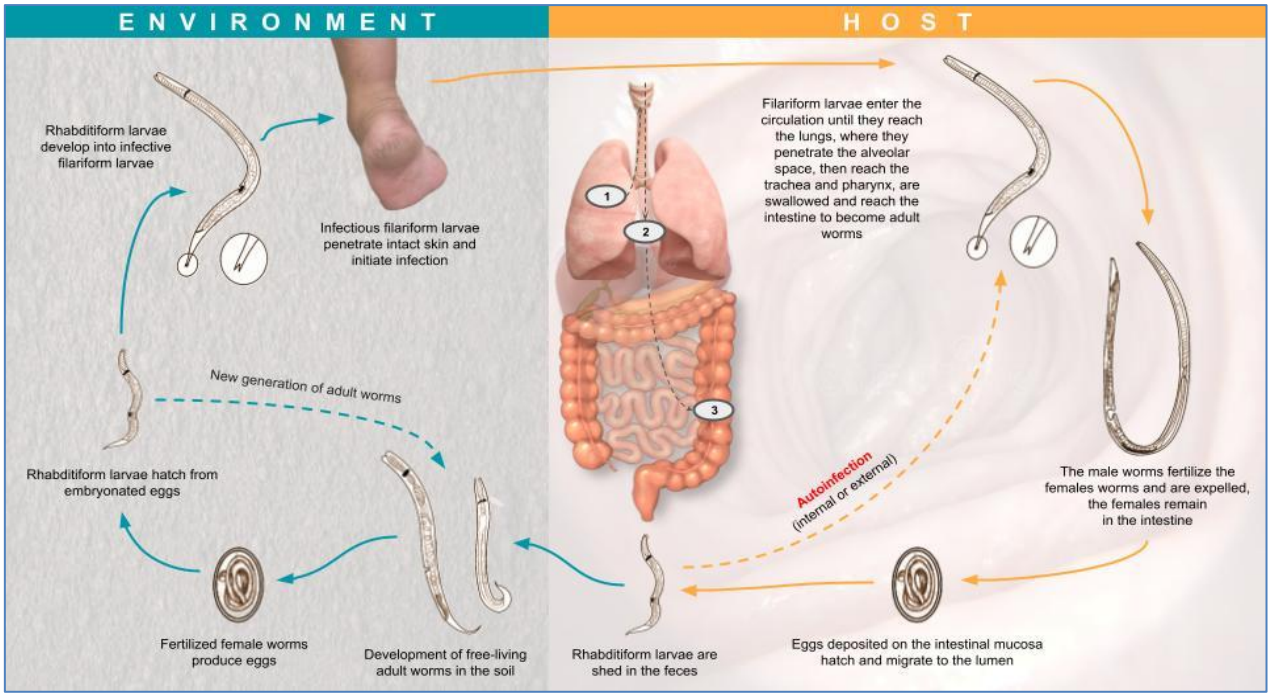

Figure 3: Biological cycle of *S. stercoralis*. (Own elaboration adapted from the CDC, available at: https://www.cdc.gov/dpdx/strongyloidiasis/index.html , and diagrams from the Department of Microbiology and Parasitology of the Fluminense Federal University)

Until now it is considered that the occurrence of autoinfection in humans with helminth infections is recognized only in infections by *S. stercoralis* and *Capillaria philippinensis*. Autoinfection explains the possibility of persistent infections for many years, in people who have not been to an endemic area, and of hyperinfections in immunocompromised individuals [5-16].

Pathogenesis and Pathophysiology

By themselves, the larvae during their migration cause traumatic, mechanical, and inflammatory damage to the skin, intestinal mucosa, and lungs. The adult form generates the same effects, but on its definitive habitat, which corresponds to the duodenum or jejunum, in addition to being the area where there is the greatest parasite load (adults, eggs, and larvae).

Initially, when the filariform larvae penetrate the skin, they usually cause a petechial hemorrhagic rash and a significant inflammatory reaction, followed by intense pruritus, edema, and engorgement that together may favor further infections. Migration through the lymphatics and venules reaches the pulmonary circulation and produces hemorrhages in the pulmonary capillaries and bronchopneumonic exudate. The larvae advance further into the alveolar spaces and cause inflammatory responses associated with eosinophilic infiltration that ends in pneumonitis, this

because the larvae rupture the alveolar-capillary membrane during their passage. Finally, the larvae crawl through the respiratory tract and are swallowed, thus reaching the intestine, where the parasites, already in their adult form, generate a chronic inflammatory reaction and the mucosa becomes edematous and ulcerative, as well as the atrophy of villi and the appearance of lesions. Granulomatous [2- 16].

Clinical Manifestations

S. stercoralis infection can cause 5 different manifestations [23]:

1. Löeffler syndrome
2. Chronic intestinal infection
3. asymptomatic autoinfection
4. symptomatic autoinfection
5. Hyperinfection syndrome (HS) and dissemination

Acute strongyloidiasis is often asymptomatic and can remain hidden for decades. Immunocompetent patients usually have asymptomatic chronic infections that cause minor morbidity. Strongyloidiasis can clinically lead to cutaneous, pulmonary, and gastrointestinal manifestations:

- **Cutaneous strongyloidiasis:** the first manifestation of infection by this nematode is by the penetration of the filariform larva, which occurs immediately and can last from a few days to weeks, commonly called "serpiginous urticaria", "larva currens" or " crawling dermatitis", which is accompanied by pruritus and erythema; It appears mainly on the soles of the foot and legs. When these lesions heal, they generate dyschromic spots known as chilblains.
- **Pulmonary strongyloidiasis: causes the so-called** Löeffler syndrome, the same entity caused by other helminths such as *A. lumbricoides, N. americanus* or *A. duodenale*, in which the rupture of the alveolar-capillary membrane causes coughing, expectoration, hemoptysis and fever.
- **Gastrointestinal strongyloidiasis:** it can progress asymptomatically to other clinical pictures characterized by diarrhea, epigastric and abdominal pain, anorexia, vomiting, constipation, etc [2-12].

The phases of the disease have a related clinical picture according to the evolution. (TABLE 2)

Table 2: Symptoms and signs of strongyloidiasis

Phase	Clinical Manifestations
Acute	Larva currens Itching (usually in the feet) Wheezing/coughing/low-grade fever Epigastric pain Diarrhoea/nausea/vomiting
Chronic	Larva currens Epigastric pain Asymptomatic or vague abdominal discomfort Intermittent diarrhea (alternating with constipation) occasional nausea and vomiting Weight loss Recurring skin rashes (chronic urticaria)
Severe (Hyperinfection and dissemination syndrome)	Insidious installation Diarrhea (occasionally bloody) Severe abdominal pain, nausea, and vomiting Cough, wheezing, functional respiratory syndrome Neck stiffness, headaches, confusion (meningismus) Skin rash (petechiae, purpura) Fever and chills

Acute and chronic strongyloidiasis have a good prognosis, however, untreated infection can persist for the rest of the patient's life due to the previously mentioned cycle of autoinfection. On the other hand, disseminated infection is frequently a fatal event, and often does not respond to treatment [2- 16].

Diagnosis

The diagnosis is not easy, it should be suspected in patients residing in endemic areas with gastrointestinal, pulmonary and/or dermatological symptoms. Diagnostic methods include:

1. Direct Visualization of Larvae by:

a) Microscopy of biological material (faeces, sputum, bronchoalveolar lavage, CSF)

b) Microscopy of tissue biopsies

2. Serological tests (IFA, IHA, EIA, ELISA)

3. Molecular tests (RT-PCR)

Agar plate culture is considered the gold standard, it has a sensitivity of up to 90%, however its low availability limits its use for research purposes. Within the conventional parasitological techniques, the Baermann method and Harada-Mori culture are useful, however, it is important to note that they have low sensitivity because the nematode load is usually low and fluctuating, and several analyzes are needed. of fecal matter to reach a conclusive diagnosis. [11].

Coproparasitoscopic examinations (CPS) are useless, since the eggs of this nematode are almost never found because the parasitizing female deposits them in the intestinal mucosa, crypts and/or glands. A single sample for CPS has a sensitivity value around 30%, 3 samples approximately 70% and 7 samples a value close to 100% [24]. Visualization of eggs is evidenced by duodenal biopsies, in which it is also common to find ulcerated mucosa, neutrophilic infiltration, and even the presence of rhabditoid larvae [2- 11]. Other less frequently described options include the use of duodenal aspirate and Beal's capsule [20].

Sputum cytology processed with Papanicolau staining is a non-invasive and cost-effective method capable of showing parasite specimens, it is used in the pulmonary and gastrointestinal form.

Laboratory tests may reveal eosinophilia, hypoalbuminemia, anemia, and decreased hematocrit. In disseminated forms, translocation of bacteria by larvae into their cuticle, cerebrospinal fluid (CSF) cultures, and blood culture may reveal Gram-negative coinfections [11- 21].

Differential Diagnosis

Some other conditions cause symptoms similar to strongyloidiasis, including:

- Intestinal infections: amoebiasis, bacterial colitis, infection by *Shigella* spp., *Yersinia* spp., *Campylobacter jejuni*, *Clostridium difficile*, *Blastocystis* spp., etc.
- Functional gastrointestinal disorders (irritable bowel syndrome, functional dyspepsia, abdominal migraine, etc.)
- Adverse drug effects (NSAIDs)

Regarding skin lesions, the differential diagnosis should be considered with other causes of skin lesions such as cutaneous larva migrans (CML), filariasis or dracunculiasis, taking into account the different prevalence according to geographical areas.

Finally, hyperinfection syndrome should be considered in the differential diagnosis of any immunosuppressed patient, in addition to pictures of bacteremia due to *S. pyogenes* or shock of unclear origin [2- 18].

Treatment

Currently no public health strategy has been developed. This condition has decreased its prevalence in countries where sanitation and human waste disposal has improved. In some areas, massive treatment with ivermectin to control onchocerciasis or lymphatic filariasis probably reduces it, however, there is no information on this [25].

According to the Centers for Disease Control and Prevention (CDC), treatment should be administered as appropriate to the symptoms of acute, chronic strongyloidiasis, and hyperinfection syndrome or disseminated strongyloidiasis. (TABLE 3)

Table 3: Treatment of *S. stercoralis* infection

***S. stercoralis* infection**		
Acute and chronic strongyloidiasis	First line	Ivermectin Single dose, 200 μg/kg PO
	Relative contraindications	Confirmed or suspected manufacturing of *Loa loa* (endemic to West and Central Africa, people weighing <15 kg, pregnant or lactating.
	Alternative	albendazole 400 mg PO twice a day for 7 days
	Relative contraindications	Hypersensitivity to benzimidazole compounds or during the first trimester of pregnancy.
Disseminated strongyloidiasis and hyperinfection syndrome	Recommended	Interrupt or reduce immunosuppressive therapy if possible. Combination of antibiotic treatment for probable systemic sepsis, plus treatment with Ivermectin (200 μg/kg PO per day until stool and/or sputum tests are negative for 2 weeks).

Ivermectin is effective against the adult, but less effective on the larval and egg stages at the tissue level and in view of the autoinfectious cycle, administration of additional oral rounds of ivermectin could be implemented to eliminate females, but further quantitative studies are required. High sensitivity and precision to monitor therapy. There are no parenteral presentations available with a license for use in humans, it has been used when enteral absorption is decreased in patients with paralytic ileus or critically ill, so subcutaneous or rectal administration has been attempted as a complement or alternative [3- 21].

DISCUSSION

This parasitic disease affects millions of people around the world and has been classified as a neglected disease and a public health problem in many regions, including Mexico. Strongyloidiasis is a common infection in areas with poor sanitary conditions and limited access to health services. In Mexico, it has been observed that the disease is more prevalent in rural areas and in communities with low resources. It is important to note that until the last quarter of 2022, 40.1% of the population is in conditions of working poverty [26], addition that this is not a mandatory reportable disease.

People can contract the infection through direct contact with soil contaminated with parasite larvae. The symptoms of strongyloidiasis can range from mild to severe as in the case of hyperinfection syndrome. The importance of this parasite lies in the fact that the distinctive characteristic of internal autoinfection contributes to chronicity and difficulty in controlling the infection. This cycle of autoinfection can be especially problematic in immunocompromised individuals, such as those with HTLV-1, HIV/AIDS, or under immunosuppressive treatment, as they can develop severe and disseminated infections by the parasite with fatal consequences.

Proper and timely diagnosis is essential to control the disease and prevent complications. However, due to lack of awareness and resources in certain areas, diagnosis can be delayed, increasing the risk of spreading the infection as well as the persistence of the agent in the environment, as in this case where only the report of 11 cases in a period of 22 years. As a neglected disease, strongyloidiasis often receives less attention from health systems and scientific research, this can lead to a lack of availability of drugs and up-to-date treatment protocols, and prevention and control can be difficult. To implement in areas with limited health infrastructures, situations that tend to be predominant in endemic areas of this disease.

CONCLUSION

The worrying situation of strongyloidiasis in the country is highlighted, underlining its forgotten nature and the lack of attention it has received. Because it is not classified as a mandatory reporting disease, the disease shows clear signs of underdiagnosis and underreporting, as evidenced by the limited 11 cases reported in the last two decades. This pattern may have significant public health consequences, and strongyloidiasis is of research interest because of its ability to persist in the body for long periods of time and its potential to cause chronic infections and serious complications in individuals. immunocompromised, the low number of reported cases could be underestimating the true prevalence of the disease in the Mexican population, which could be masking its true impact on public health.

Lack of awareness about strongyloidiasis leads to late diagnosis or lack of adequate treatment in infected individuals. This not only increases the individual burden of disease but can also contribute to the spread of infection in the environment and in the community. In addition, the lack of accurate data on the incidence and prevalence of strongyloidiasis makes it difficult to implement effective prevention and control strategies. To address strongyloidiasis as a public health problem in Mexico, comprehensive efforts are needed that include: 1) awareness and education among the population and health professionals; 2) improvement of health infrastructure and improvement of access to medical services in rural areas and low-income communities; 3) research and development of effective and safe treatments; and 4) prevention strategies and their implementation, such as the improvement of basic sanitation and hygiene.

In short, the need to pay attention to strongyloidiasis in Mexico is highlighted, recognizing its traditionally forgotten character and calling attention to the importance of improving epidemiological surveillance and diagnosis of this disease. It is crucial that awareness is promoted both among health professionals and the general population in order to adequately address strongyloidiasis and mitigate its impact on public health in Mexico.

CONFLICT OF INTEREST: The authors declare that they have no conflict of interest.

CONTRIBUTION OF AUTHORS:

All authors contributed to the conception/design of the work, data/information collection, analysis /discussion of the data, bibliographic review, preparation of the manuscript, and review of the final version.

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